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EXAMINER

PRASAD, S

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

10/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Applicati n N .

09/532,263

Applicant(s)

Hilton, Douglas James

Examiner

Sarada C Prasad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-5,8,9,11-15,17-21,24-26,28-29 is/are pending in the application.
- 4a) Of the above claim(s) 13-15,17-21,24-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,8,9,11,12,26,28-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Restriction/Election

1. Applicant's election with traverse of Group I (claims 1, 3-5, 8-9, 11-12, 26, 28-29) in Paper No. 5 (8/2/01) is acknowledged. The traversal is on the ground(s) that restriction of instant claims into three groups based on different classification is not justified. This is not found persuasive because: while classification is one of the ways to distinguish the distinctness of claims it is certainly not the only reason why the Examiner divided the instant claims into three patentably distinct groups. In fact, the Examiner has provided the reasons for the distinctness of the three groups as follows: Group I drawn to a nucleic acid that can be used either as a hybridization probe, or to make the specific protein, or in gene therapy, while the protein of invention II can be made by more than one method such as by recombinant methods using the polynucleotide of the invention, or by purification from tissue sources, or by chemical means. At the same time, the invention of Group III, directed to identification and cloning of the IL-11 receptor, can be achieved in more than one way (pages 2-3 of Paper No. 4, 6/29/01).

The traversal is also on the grounds that (i) Groups I-III are interrelated and interdependent rather than 'independent and distinct', and (ii) examination of the entire application or at least Groups I and III would not constitute a burden to search (page 3 of Applicant's remarks, Paper No.5, 8/2/01). This is not found persuasive because with respect to point (i) above, the inventions are distinct as noted in the last office action, and as shown by the distinctness described therein. Applicant's attention is directed to MPEP 806.05. With respect to point (ii) above, contrary to applicants' assertion that any search of the prior art in regard to invention of Group I will reveal whether any prior art exists as to the other Groups, a search is directed to references which would render the invention obvious, as well as references directed

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to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. Additionally, the commonality in Groups I and III is entirely based on hybridization methodology and the specificities with which the cDNAs select genomic DNAs encoding the same polypeptides. In the instant case the recombinant DNAs are highly modified, fragments, derivatives, homologues, analogues with the result that the searches would only be partially complete requiring additional searches posing a burden for the Examiner. Therefore the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 2, 6-7, 10, 16, 22-23, and 27 have been cancelled, claims 13-15, 17-21, 24-25 are withdrawn from consideration as being non-elected, and currently claims 1, 3-5, 8-9, 11-12, 26, 28-29 are under consideration for examination.

Detailed Action

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: the instant application claims priority to an earlier application with serial no. 08/702,665 filed on 12/20/1996 while the declaration recites the filing date as 9/9/1996. Appropriate correction is required. Furthermore, the first line of specification recites the filing date of the earlier application with serial no. 08/702,665 as 9/5/1995 instead of 12/20/1996.

2b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. A suggested title would be 'Human Interleukin-11 receptor'. Furthermore, use of the term 'novel' in the title is objected to because all inventions are novel and that term in the title would be redundant.

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Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1, 3, 4, 5, 8, 9, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule of SEQ ID No. 4 which encodes an α chain of human IL-11 receptor having an amino acid sequence comprising SEQ ID NO. 5, does not reasonably provide enablement for an isolated nucleic acid molecule comprising a sequence of nucleotides encoding an IL-11 receptor α chain mutant, derivative, component, part, fragment, homologue, analogue, or a peptide or a polypeptide equivalent thereof wherein said IL-11 receptor comprises an amino acid sequence set forth in SEQ ID No. 1; or an isolated polynucleotide capable of hybridizing to SEQ ID no. 4 under low stringency conditions; or an isolated nucleic acid molecule encoding a mammalian IL-11 receptor α chain, said nucleic acid molecule further defined by the ability of an oligonucleotide of SEQ ID No. 6-10 to hybridize thereto under medium stringency conditions, or a complement thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specifications sets forth an amino acid sequence of SEQ ID No.5 as representing the IL-11 receptor α chain, and an isolated nucleic acid of SEQ ID No.4 encoding the same (specification page 4, 2nd para, lines 6-8). SEQ ID No. 5 also comprising an amino acid sequence set forth in SEQ ID No. 1: Trp-Ser-Xaa-Trp-Ser (residues 305 to 309).

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Claim 1 is overly broad in the recitation of an isolated nucleic acid molecule comprising a sequence of nucleotides encoding, or complementary to a sequence encoding an IL-11 receptor or a mutant, derivative, component, part, fragment, homologues, analogue or a peptide or polypeptide equivalent thereof when said IL-11 receptor comprising an amino acid sequence as set forth in SEQ ID No. 1, which is Trp-Ser-Xaa-Trp-Ser, because the claim language encompasses innumerable variant nucleic acids which may or may not encode an IL-11 receptor with the penta-peptide 'Trp-Ser-Xaa-Trp-Ser' included in it. The specification is not enabled for preparation of variant nucleic acids and complement thereof of undefined mutants, derivatives, components, parts, fragments, homologues, analogues because sufficient guidance is not provided to generate the variants that meet the limitations of the instant claim. It requires undue experimentation for one of skill in the art to figure out 'what is included and what is not' from the myriad of possible changes in the nearly 1800 base long nucleic acid encoding IL-11 receptor that can be possibly generated and tested for functionality.

Claim 9 is overly broad in the recitation of a complementary nucleic acid sequence that is capable of hybridizing to SEQ ID No. 4 under low stringency conditions, encompassing both sense and anti-sense strands of the several variant nucleic acids encoding IL-11 receptor. The specification is also not enabled for such nucleic acid variants of SEQ ID No. 4 because the number of such nucleic acid molecules is too large to identify which of them would prove to be useful to screen for muteins of IL-11 receptor.

Claim 12 is extremely broad in reciting an isolated nucleic acid molecule encoding a mammalian IL-11 receptor α chain further defined by the ability of an oligonucleotide (SEQ ID No. 6-10) to hybridize, under medium stringency conditions or a complement of it. The

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specification is also not enabled for such nucleic acid molecules because there is not enough guidance to make certain that any of these nucleic acids will encode a polypeptide with characteristic features of the IL-11 receptor.

Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, is it undue (In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404).

Therefore, considering the breadth of claims 1, 9, and 12, state-of-the-art suggesting how critical is each amino acid residue when generating variants, lack of sufficient guidance in the

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specification for generating specific variants of the claimed genus, the amount of experimentation required is undue to practice the invention as claimed.

Claims 3-5, 8, and 11 are rejected insofar as they depend on claims 1, 9, and 12.

3b. Claim 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant specifications sets forth SEQ ID Nos. 6-10 as oligonucleotide probes for selecting a genetic sequence based on hybridization (page 4, last para, lines 4-end of page). Each of these five 15-mer oligonulceotide probes of SEQ Nos. 6-10, or the corresponding complementary sequences have choices for alternate nucleotide residues (in positions 1, 7, and 10) thus making the number of probes that these SEQ IDs 6-10 represent really several more than just five. Thus the probes are not of definite sequence.

The specification is not enabling for practice of claims 26-28 because such indefinite probes of SEQ ID Nos. 6-10, when hybridized to a genetic sequence under medium stringency conditions would hybridize to a myriad of sequences out of which the probability of any one of them representing the instant IL-11 receptor variant is a matter of chance.

3c. Claims 1, 3-5, 9, 11-12, 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The instant written description sets forth a polynucleotide of SEQ ID No. 4 (1800 nucleotides long) encoding an amino acid sequence of SEQ ID No.5 (423 amino acid residue) representing the IL-11 receptor α chain (specification page 4, 2nd para, lines 6-8) which also comprises SEQ ID No. 1: Trp-Ser-Xaa-Trp-Ser (residues 305 to 309). However, the written description is not commensurate with an isolated nucleic acid molecule comprising a sequence of nucleotides encoding an IL-11 receptor mutant, derivative, component, part, fragment, homologue, analogue, or a peptide or a polypeptide equivalent thereof wherein said IL-11 receptor comprises an amino acid sequence set forth in SEQ ID No. 1; or an isolated polynucleotide capable of hybridizing to SEQ ID No. 4 under low stringency conditions; or an isolated nucleic acid molecule encoding a mammalian IL-11 receptor chain, said nucleic acid molecule further defined by the ability of an oligonucleotide of SEQ ID No. 6-10 to hybridize thereto under medium stringency conditions, or a complement thereof.

Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the claimed invention. Therefore, the Applicant is not in possession of the invention as claimed, at the time of filing. This is insufficient to support the claims as provided by the Revised Written description Guidelines published in the Federal register, vol 66, No.4, pages 1099-1111, Friday January 2001.

Instant specification provides general principles for making the polypeptide variants of SEQ ID No. 4 (pages 2-12). The specification suggests generalized method for cloning hematopoietin receptors, in particular component chains thereof which provide a basis for developing a range of agonists, antagonists, therapeutic and diagnostic agents based on the IL-11 receptor (page 2, 2nd para, lines 7-11). However, the disclosure fails to provide detailed

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description directed to the intended specific variants of the 423 amino acid residue protein. It is not sufficient to name the claimed variant nucleic acids comprising mutants, derivatives, homologues, analogues, components, or complement of nucleic acid of SEQ ID No. 4 hybridizing under low stringency conditions (as claimed in claims 1, 9, 12) without actually generating any of the said variants, and demonstrating their proper membership in the claimed genus.

Additionally, none of the proposed 'sequence variants' have been shown to be successfully achieved by the claimed amino acid changes to SEQ ID No. 4 with deletions, replacements or substitutions of amino acid residues, while retaining the amino acid sequence set forth by SEQ ID No.1, and yet have any of the features/properties and biological activity characteristic of the intended putative IL-11 receptor α chain. Since the disclosure fails to describe successful generation of any such variants with expected criteria, or describe what are the many permitted amino acid changes while preparing variants of SEQ ID No. 4, it can be reasonably concluded that Applicant is not in possession of the claimed variants at the time of filing.

The genus is highly variant and the disclosure of a specific polypeptide sequence is insufficient to describe the genus consisting of portions, small pieces or fragments of SEQ ID No.4, complementary sequences that encode for a protein, or fragments that are potentially useful as agonists, antagonists, therapeutic and diagnostic agents. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species sufficient to describe and enable the genus as broadly claimed.

Claims 3-5, 9, 11 are rejected insofar as they depend on claim 1.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 9 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 9 and 26 are vague and indefinite in reciting the phrase 'capable of' because use of the instant phrase fails set forth the range or the limits of the conditions under which the said hybridizing is expected to occur or not occur. In other words the limitations following the phrase are uncertain.

4b. Claim 1 is vague and indefinite in reciting 'derivative, component, part fragment homologues analogue polypeptide equivalent thereof'. It is not clear as what are the variants, derivatives, components, fragments, homologues, analogues, polypeptide equivalent thereof because use of such terms without fragment delimiters fails to define what is intended in the list of putative variants of IL-11 receptor α chain.

4c. Claim 9 and 12 recite phrases such as 'under low stringency conditions' or 'under medium stringency conditions' which are relative and conditional terms rendering the claims indefinite. Furthermore, some nucleic acids which might hybridize under moderate stringency, for example, would fail to hybridize at all under conditions of high stringency. The metes and bounds of the claims thus can not be ascertained. This rejection can be obviated by supplying the specific conditions supported by the specification which applicants consider to be 'stringent'.

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Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5a. Claims 1, 3, 4, 5, 8, 9, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/19574 (27th June 1996).

WO 96/19574 (27th June 1996) teaches polynucleotides encoding the human IL-11 receptor comprising the sequence and fragments thereof, which also comprises the amino acid sequence of Trp-Ser-Xaa-Trp-Ser (residues 313-317, page 39 of WO 96/19574) as set forth in the instant SEQ ID No. 1, soluble receptors, methods for their production, and identification (abstract, lines 1-2). Also taught are fragments of amino acids sequence of SEQ ID No. 2 from 24-422, 24-365, 391-422, 102-422, 102-365, having biological activity of the human IL-11 receptor (claim 13, page 46) thus meeting the limitations of instant claims 1, 3, 4, 5, 8, 9, 11 (see the attached sequence alignment A).

5b. Claims 12 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorman et al. (1992).

Gorman et al. teach oligonucleotide probes that have 92% global and 80% local similarity to SEQ ID No. 6 (see sequence alignment B) which meets the limitations of instant claims 12 and 29 in setting forth oligonucleotide probes of instant SEQ ID No. 6-10 (specification, page 4) for selection of sequences that encode IL-11 receptor α chain from genetic sequences.

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Conclusion

6. No claims are allowed.


Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday - Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
October 4th, 2001


YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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